In the Specification:

Please replace the paragraph beginning at page 58 line 18, with the following amended paragraph:

Cloning of *dnaX* - DNA oligonucleotides for amplification of *T.th.* genomic DNA were as follows. The upstream 32mer (5'-CGCAAGCTTCACGCSTACCTSTTCTCCGGSAC-3') (SEQ ID NO: 6) (S indicates a mixture of G and C) consists of a Hind III site within the first 9 nucleotides (underlined) followed by codons (SEQ ID NO: 29) encoding the following sequence (HAYLFSGT) (SEQ ID NO: 7). The downstream 34 mer (5'-CGCGAATTCGTGCTCSGGSGGCTCCTCSAGSGTC-3') (SEQ ID NO: 8) consists of an EcoRI site (underlined) followed by codons encoding the sequence KTLEEPPEH (SEQ ID NO: 9) on the complementary strand. The amplification reactions contained 10 ng *T.th.* genomic DNA, 0.5 mM of each primer, in a volume of 100 µl of Vent polymerase reaction mixture according to the manufacturers instructions (10 µl ThermoPol Buffer, 0.5 mM each dNTP and 0.5 mM $MgSO_4$). Amplification was performed using the following cycling scheme: 5 cycles of: 30 s at 95.5°C, 30 s at 40°C, 2 min. at 72°C; 5 cycles of: 30 s at 95.5°C, 30 s at 45°C, and 2 min. at 72°C; and 30 cycles of: 30 s at 95.5°C, 30 s at 50°C, and 30 s at 72°C. Products were visualized in a 1.5 % native agarose gel.

Please replace the paragraph beginning at page 63, line 1, with the following amended paragraph:

Assuming the first stop codon is utilized (i.e. -2 frameshift), the predicted size of the γ subunit in *T.th.* is 454 amino acids for a mass of 49.8 kDa, over 2 kDa larger than the 431 residue γ subunit (47.5 kDa) of *E. coli*. This would result in 2 residues after the -2 frameshift (i.e. after the GluLysLys, the residues LysAla would be added) to be compared to the result of the -1 frameshift in *E. coli* which also results in 2 residues (LysGlu). In the event that a -1 frameshift were utilized in the *T.th. dnaX* gene, then an additional 12 residues would be added following the frameshift for a molecular mass of 50.8 kDa (i.e. after the GluLysLys, the residues LysProAspProLysAlaProProGlyProThrSer (SEQ ID NO: 18) would be added).

As explained later, this nucleotide sequence was found to promote both -1 and -2 frameshifting in *E. coli* (Fig. 8). But first, we examined *T.th.* cells by Western analysis for the presence of two subunits homologous to *E. coli* γ and τ.

Please replace the paragraph beginning at page 63, line 25, with the following amended paragraph:

The upstream primer for the shifty sequences was 5'-gcg cgg atc cgg agg gag aaa aaa aaa gcc tca gcc ca-3' (SEQ ID NO: 10). The BamHI site for cloning into pUC is underlined. Also, the stop codon, tga, has been mutated to tca (also underlined). The upstream primer for the mutant shifty sequence was: 5'-gcg cgg atc cgg agg gag aga aga aaa gcc tca gcc ca-3' (SEQ ID NO: 11). The mutant sequence contains two substitutions of a G for an A residue in the polyA stretch (underlined). Three downstream primers were utilized with each upstream primer to create two sets of three inserts in the 0 frame, -1 frame and -2 frame. The sequence of these primers, and the length of insert (after cutting with EcoRI and BanHI and inserting into pUC19) are as follows: 5'-gaa tta aat tcg cgc ttc ggg agg tgg g-3' (SEQ ID NO: 12) (0 frameshift, total 58 nucleotide insert); 5'-gcg cga att cgc gct tcg gga ggt ggg-3' (SEQ ID NO: 13)(-1 frame, 54mer insert); and 5'-gcg cga att cgg gcg ctt cag gag gtg gg-3' (SEQ ID NO: 14) (-2 frame, 56mer insert). The downstream primers have an EcoRI site (underlined); the EcoRI site of the 0 frame insert was blunt ended to produce the greater length insert (converting the EcoRI site to an aattaatt sequence). Also, the tcg sequence, which produces the tga stop codon (underlined) was mutated to tca in the -2 downstream primer so that readthrough would be allowed after the frameshift occurred.

Please replace the paragraph beginning at page 65, line 3, with the following amended paragraph:

The dnaX gene was cloned into the pET16 expression vector in the steps shown in Fig. 9. First, the bulk of the gene was cloned into pET16 by removing the PmlI/XbaI fragment from pAlterdnaX, and placing it into SmaI/XbaI digested Puc19 to yield Puc19dnaXCterm. The N-terminal sequence of the dnaX gene was then reconstructed to position an NdeI site at the N-terminus. This was performed by amplifying the 5' region encoding the N-terminal section of γ/τ using an upstream primer containing an NdeI site that hybridizes to the dnaX gene at

the initiating gtg codon (i.e. to encode Met where the Met is created by the PCR primer, and the Val is the initiating gtg start codon of *dnaX*). The primer sequence for this 5' end was: 5'-gtggtgcatatg gtg agc gcc ctc tac cgc c-3' (SEQ ID NO: 15)(where the NdeI site is underlined, and the coding sequence of *dnaX* follows). The downstream primer hybridizes past the PmlI site at nucleotide positions 987 - 1004 downstream of the initiating gtg (primer sequence: 5'-gtggtggtcgac cca gga ggg cca cct cca g-3' (SEQ ID NO: 16) where the initial 12 nucleotides contain a SalGI restriction site, followed by the sequence from the region downstream the stop codon). The 1.1 kb nucleotide PCR product was digested with PmlI/NdeI and the PmlI/NdeI fragment was ligated into NdeI/PmlI digested Puc19dnaXCterm to form Puc19dnaX. The Puc19dnaX plasmid was then digested with NdeI and SalI and the 1.9 kb fragment containing the dnaX gene was purified using the Sephaglas BandPrep Kit (Pharmacia-LKB). pET16b was digested with NdeI and XhoI. Then the full length dnaX gene was ligated into the digested pET16b to form pET*dnaX*.

Please replace the paragraph beginning at page 71, line 20, with the following amended paragraph:

The XbaI insert encoded an open reading frame, starting with a GTG codon, of 529 amino acids in length (58.0 kDa), closer to the predicted length of the *B. subtilis* τ subunit (563 amino acids, 62.7 kDa mass)(Alonso et. al., 1986) than the *E. coli* τ subunit (71.1 kDa)(Yin et. al., 1986). *dnaX* encoding the γ/τ subunits of *E. coli* DNA polymerase III holoenzyme is homologous to the *holB* gene encoding the δ' subunit of the γ complex clamp loader, and this homology extends to all 5 subunits of the eukaryotic RFC clamp loader as well as the bacteriophage gene protein 44 of the gp44/62 clamp loading complex (O'Donnell et. al., 1993). These gene products show greatest homology over the N-terminal 166 amino acid residues (of *E. coli* dnaX); the C-terminal regions are more divergent. Fig. 4 shows an alignment of the amino acid sequence of the N-terminal regions of the *Tth* dnaX gene product to those of several other bacteria. The consensus GXXGXGKT (SEQ ID NO: 17) motif for nucleotide binding, is conserved in all these protein products. Further, the *E. coli* δ' crystal structure reveals one atom of zinc coordinated to four Cys residues (Guenther, 1996). These four Cys residues are conserved in the *E. coli dnaX* gene, and the γ and τ subunits encoded by *E. coli* dnaX bind one atom of zinc (J. Turner and M. O'Donnell, unpublished). These Cys

residues are also conserved in *Tth* dnaX (shown in Fig. 4). Overall, the level of amino acid identity relative to *E. coli* dnaX in the N-terminal 165 residues of *Tth* dnaX is 53 %. The *Tth dnaX* gene is just as homologous to the *B. subtilis* dnaX (53 % identity) gene relative to *E. coli* dnaX. After this region of homology, the C-terminal region of *Tth* dnaX shares 26% and 20% identity to *E. coli* and *B. subtilis* dnaX, respectively. A proline rich region, downstream of the conserved region, is also present in *Tth* dnaX (residues 346-375), but not in the *B. subtilis* dnaX (see Figs. 3A and 3B). The overall identity between *E. coli* dnaX and *Tth* dnaX over the entire gene is 34%. Identity of *Tth*. dnaX to *B. subtilis* dnaX over the entire gene is 28%.

Please replace the paragraph beginning at page 78, line 14, with the following amended paragraph:

Cloning of the *dnaE* gene was started with the sequence of the TTH1 peptide from the purified α subunit (FFIEIQNHGLSEQK) (SEQ ID NO: 61). The fragment was aligned to a region at approximately 180 amino acids downstream of the N-termini of several other known α subunits as shown in Fig. 15. The upstream 33mer (5'-GTGGGATCCGTGGTTCTGGATCTCGATGAAGAA-3') (SEQ ID NO: 31) consists of a BamHI site within the first 9 nucleotides (underlined) and the sequence coding for the following peptide HGLSEQK (SEQ ID NO.: 117) on the complementary strand. The downstream 29mer (5'-GTGGGATCCACGGSCTSTCSGAGCAGAAG-3') (SEQ ID NO: 32) consists of a BamHI site within the first 9 nucleotides (underlined) and the following sequence coding for the peptide FFIEIQNH (SEQ ID NO: 62).

Please replace the paragraph beginning at page 79, line 13, with the following amended paragraph:

The upstream 34mer (5'-GCGGGATCCTCAACGAGGACCTCTCCATCTTCAA-3') (SEQ ID NO: 33) consists of a BamHI site within the first 9 nucleotides (underlined) and the sequence from the end of the fragment previously obtained. The downstream ~~33mer~~ 35mer (5'-GCGGGATCCTTGTCGTCSAGSGTSAGSGCGTCGTA-3') (SEQ ID NO: 34) consists of a BamHI site within the first 9 nucleotides (underlined) and the following sequence coding for the peptide YDALTLDD on the complementary strand. The amplification reactions

contained 10 ng *T.th.* genomic DNA, 0.5 mM of each primer, in a volume of 100 µl of Vent polymerase reaction mixture containing 10 µl ThermoPol Buffer, 0.5 mM of each dNTP and 0.25 mM Mg SO_4. Amplification was performed using the following cycling scheme:

1. 4 cycles of: 95.5°C - 30", 45°C - 30", 75°C - 8'
2. 6 cycles of: 95.5°C - 30", 50°C - 30", 75°C - 6'
3. 30 cycles of: 95.5°C - 30", 55°C - 30", 75°C - 5'

A 1.2kb PCR fragment was obtained and cloned into pUC19:BamHI. The fragment was bracketted by the downstream primer on both sides and contained the region overlapping in 56 bp with the fragment previously cloned.

Please replace the paragraph beginning at page 80, line 4, with the following amended paragraph:

To obtain yet more *dnaE* sequence, the following primers were used. The upstream 39mer (3'-GTGTGGATCCTCGTCCCCCTCATGCGCGACCAGGAAGGG-5') (SEQ ID NO: 114) consists of a BamHI site within the first 10 nucleotides (underlined) and the sequence from the end of the fragment previously obtained. The downstream 27mer (5'-GTGTGGATCCTTCTTCTTSCCCATSGC-3') (SEQ ID NO: 36) consists of a BamHI site within the first 10 nucleotides (underlined), and the sequence coding for the peptide AMGKKK (SEQ ID NO: 64) (at position approximately 800 residues from the N terminus) on the complementary strand. The AMGKKK (SEQ ID NO: 64) sequence was chosen for primer design as it is highly conserved among the known gram-negative α subunits. The amplification reactions contained 10 ng *T.th.* genomic DNA, 0.5 mM of each primer, in a volume of 100 µl of Taq polymerase reaction mixture containing 10 µl PCR Buffer, 0.5 mM of each dNTP and 2.5 mM $MgCl_2$. Amplification was performed using the following cycling scheme:

1. 3 cycles of: 95.5°C - 30", 45°C - 30", 72°C - 8'
2. 6 cycles of: 94.5°C - 30", 55°C - 30", 72°C - 6'
3. 32 cycles of: 94.5°C - 30", 50°C - 30", 72°C - 5'

A 2.3kb PCR fragment was obtained instead of the expected 0.6 kb fragment. BamHI digestion of the PCR product resulted in three fragments of 1.1 kb, 0.7kb and 0.5kb. The 1.1

kb fragment was cloned into pUC19:BamHI. It turned out to be the one adjacent to the fragment previously obtained and contained the *dnaE* sequence right up to the region coding for the AMGKKK (SEQ ID NO: 64) peptide, but was disrupted by an intein just upstream of this region.

Please replace the paragraph beginning at page 80, line 26, with the following amended paragraph:

The sequence that follows this was amplified from the 2.3kb original PCR product using the same conditions and cycling scheme as for the 2.3kb fragment. The downstream primer was the same as in the previous step. The upstream 27mer (3'-GTGTGGATCCGTGGTGACCTTAGCCAC-5') (SEQ ID NO: 115) consisted of a BamHI site within the first 9 nucleotides (underlined) and the sequence from the end of the 1.1kb fragment previously described.

Please replace the paragraph beginning at page 81, line 5, with the following amended paragraph:

The expected 1.2kb PCR fragment was obtained and cloned into pUC19:SmaI. This fragment coded for the rest of the intein and the end of it was used to obtain the next sequence of *dnaE* downstream of this region. The upstream 30mer (3'-TTCGTGTCCGAGGACCTTGTGGTCCACAAC-5') (SEQ ID NO: 116) was a sequence from the end of the intein. The downstream 23mer (5'-CCAGAATCGTCTGCTGGTCGTAG-3') (SEQ ID NO: 39) was the sequence from the end of the *dnaE* gene of *D.rad.* (coding on the complementary strand for the region slightly homologous in the distantly related α subunits and possibly highly homologous between *T.th.* and *D.rad.* α subunits). The amplification reactions contained 10 ng *T.th.* genomic DNA, 0.5 mM of each primer, in a volume of 100 µl of Vent polymerase reaction mixture containing 10 µl ThermoPol Buffer, 0.5 mM of each dNTP and 0.1 mM Mg SO_4. Amplification was performed using the following cycling scheme:

1. 3 cycles of: 95.5°C - 30", 55°C - 30", 75°C - 8'
2. 32 cycles of: 94.5°C - 30", 50°C - 30", 75°C - 5'

A 2.5kb PCR fragment was obtained and cloned into pUC19:SmaI. This fragment contained the dnaE sequence coding for the 300 ~~mino~~ amino acids next to the AMGKKK (SEQ ID NO: 64) region disrupted by yet a second intein inside another sequence that is conserved among the known α subunits (FNKSHSAAY) (SEQ ID NO: 65).

Please replace the paragraph beginning at page 81, line 24, with the following amended paragraph:

To obtain the rest of the *dnaE* gene the upstream 19mer (5'-AGCACCCTGGAGGAGCTTC-3') (SEQ ID NO: 40) from the end of the known *dnaE* sequence was used. The downstream primer was: 5'-CATGTCGTACTGGGTGTAC-3' (SEQ ID NO: 41). The amplification reactions contained 10 ng *T.th.* genomic DNA, 0.5 mM of each primer, in a volume of 100 µl of Vent polymerase reaction mixture containing 10 µl ThermoPol Buffer, 0.5 mM of each dNTP and 0.1 mM Mg SO_4. Amplification was performed using the following cycling scheme:

1. 3 cycles of: 95.5°C - 30", 55°C - 30", 75°C - 8'
2. 32 cycles of: 94.5°C - 30", 50°C - 30", 75°C - 5'

A 1.0kb fragment bracketed by this upstream primer was obtained. It contained the 3' end of the *dnaE* gene.

Please replace the paragraph beginning at page 82, line 17, with the following amended paragraph:

The regions highly conservative among Pol III exonucleases were chosen to design the degenerate primers for the amplification of a *T.th. dnaQ* internal fragment (see Fig. 17). DNA oligonucleotides for amplification of *T.th.* genomic DNA were as follows. The upstream 27mer (5'-GTSGTSNNSGACNNSGAGACSACSGGG-3') (SEQ ID NO: 42) encodes the following sequence (VVXDXETTG) (SEQ ID NO: 66). The downstream 27mer (5'-GAASCCSNNGTCGAASNNGGCGTTGTG-3') (SEQ ID NO: 43) encodes the sequence HNAXFDXGF (SEQ ID NO: 67) on the complementary strand. The amplification reactions contained 10 ng *T.th.* genomic DNA, 0.5 mM of each primer, in a volume of 100 µl of Vent

polymerase reaction mixture containing 10 µl ThermoPol Buffer, 0.5 mM of each dNTP and 0.5 mM $MgSO_4$. Amplification was performed using the following cycling scheme:

1. 5 cycles of: 95.5°C - 30", 40°C - 30", 72°C - 2'
2. 5 cycles of: 95.5°C - 30", 45°C - 30", 72°C - 2'
3. 30 cycles of: 95.5°C - 30", 50°C - 30", 72°C - 30"

Products were visualized in a 1.5 % native agarose gel. A fragment of the expected size of 270 bp was cloned into the SmaI site of pUC19 and sequenced with the CircumVent Thermal Cycle DNA sequencing kit accordinig to the manufacturer's instructions (New England Biolabs).

Please replace the paragraph beginning at page 83, line 16, with the following amended paragraph:

DNA oligonucleotides for amplification of *T.th.* genomic DNA were the following. The upstream 27mer (5'-CGGGGATCCACCTCAATCACCTCGTGG-3') (SEQ ID NO: 44) consists of a BamHI site within the first 9 nucleotides (underlined) and the sequence complementary to 42-61bp region of the previously cloned *dnaQ* fragment. The downstream 30mer (5'-CGGGGATCCGCCACCTTGCGGCTCCGGGTG-3') (SEQ ID NO: 45) consists of a BamHI site within the first 9 nucleotides (underlined) and the sequence corresponding to 240-261 bp region of the dnaQ fragment (see Fig. 17).

Please replace the paragraph beginning at page 84, line 16, with the following amended paragraph:

DNA oligonucleotides for amplification of the ApaI/religated *T.th.* genomic DNA were as follows. The upstream 31mer (5'-GCGCTCTAGACGAGTTCCCAAAGCGTGCGGT-3') (SEQ ID NO: 46) consists of a mbaI site within the first 10 nucleotides (underlined) and the sequence complementary to the region downstream of the ApaI restriction site in the newly sequenced *dnaQ* fragment. The downstream ~~31mer~~ 25mer (5'-CGCGTCTAGATCACCTGTATCCAGA-3') (SEQ ID NO: 47) consists of a XbaI site within the first 10 nucleotides (underlined) and the sequence corresponding to another region downstream of the ApaI restriction site in the newly sequenced *dnaQ* fragment. The 1.7 kb

PCR fragment was cloned into the XbaI site of the pUC19 vector and partially sequenced. The sequence of *dnaQ*, and the protein sequence of the ∈ subunit encoded by it, is shown in Fig. 18.

Please replace the paragraph beginning at page 85, line 5, with the following amended paragraph:

The entire amino acid sequence of the ∈ subunit predicted from the *T.th. dnaQ* gene aligns with the predicted amino acid sequence of the *dnaQ* genes of other organisms with only a few gaps and insertions (the first two amino acids, and four positions downstream) (Fig. 17). The consensus motifs (VVXDXETTG (SEQ ID NOS: 66 and 68), HNAXFDXGF (SEQ ID NO: 67), and HRALYD (SEQ ID NO: 70)), characteristic for exonucleases, are conserved. Overall, the level of amino acid identity relative to most of the known ∈ subunits, or corresponding proofreading exonuclease domains of gram positive PolC genes is approximately 30%. Upstream of start 1 (Fig. 17) there were stop codons in all three reading frames.

Please replace the paragraph beginning at page 85, line 13, with the following amended paragraph:

Expression of *DnaQ* - The DnaQ gene was cloned gene into the pET24-a expression vector in two steps. First, the PCR fragment encoding the N-terminal part of the gene was cloned into the pUC19 plasmid, containing the ApaI inverse PCR fragment into NdeI/ApaI sites. DNA oligonucleotides for amplification of *T.th.* genomic DNA were as follows. The upstream 33mer (5'-GCGGCGCATATGGTGGTGGTCCTGGACCTGGAG-3') (SEQ ID NO: 48) consists of an NdeI site within the first 12 nucleotides (underlined) and the beginning of the *dnaQ* gene. The downstream ~~31mer~~ 25mer (5'-CGCGTCTAGATCACCTGTATCCAGA-3') (SEQ ID NO: 49), already used for ApaI circular PCR, consists of an XbaI site within the first 10 nucleotides (underlined) and the sequence corresponding to the region downstream of the ApaI restriction site. The 2.2 kb NdeI/SalI fragment was then cloned into the NdeI/XhoI sites of the pET16 vector to produce pET24-a:*dnaQ*. The ∈ subunit was expressed in the BL21/LysS strain transformed by the pET24-a:*dnaQ* plasmid.

Please replace the paragraph beginning at page 86, line 13, with the following amended paragraph:

Identification of *dnaA* and *dnaN* - The *DnaA* genes of *E. coli* and *B. subtilis* share 58% identity at the amino acid sequence level within the ATP-binding domain (or among the representatives of gram-positive and gram-negative bacteria, evolutionary divergent organisms). Comparison of the predicted amino acid sequences encoded by *dnaA* of *E. coli* and *B. subtilis* revealed two highly conserved regions (Fig. 19). Within each of these regions, a seven amino acid sequence was used to design two oligonucleotide primers for use in the polymerase chain reaction. The DNA oligonucleotides for amplification of *T.th.* genomic DNA were as follows. The upstream 20mer (5'-GTSCTSGTSAAGACSCACTT-3') (SEQ ID NO: 50) encodes the following sequence: VLVKTHL (SEQ ID NO: 69). The downstream 21mer (5'-SAGSAGSGCGTTGAASGTGTG-3') (SEQ ID NO: 51) encodes the sequence: HTFNALL (SEQ ID NO: 71), on the complementary strand. The amplification reactions contained 10 ng *T.th.* genomic DNA, 0.5 mM of each primer, in a volume of 100 µl of Vent polymerase reaction mixture containing 10 µl ThermoPol Buffer, 0.5 mM of each dNTP and 0.5 mM $MgSO_4$. Amplification was performed using the following cycling scheme:

1. 5 cycles of: 95.5°C - 30", 45°C - 30", 75°C - 2'
2. 5 cycles of: 95.5°C - 30", 50°C - 30", 75°C - 2'
3. 30 cycles of: 95.5°C - 30", 52°C - 30", 75°C - 30"

Products were visualized in a 1.5% native agarose gel. A fragment of the expected size of 300 bp was cloned into the SmaI site of pUC19 and sequenced with the CircumVent Thermal Cycle DNA sequencing kit (New England Biolabs).

Please replace the paragraph beginning at page 87, line 21, with the following amended paragraph:

DNA oligonucleotides for amplification of recircularized *T.th.* genomic DNA were as follows. The upstream 22mer was 5'-CTCGTTGGTGAAAGTTTCCGTG-3' (SEQ ID NO: 52), and the downstream 24mer was 5'-CGTCCAGTTCATCGCCGGAAAGGA-3' (SEQ ID NO: 53). The amplification reactions

contained 5 ng *T.th.* genomic DNA, 0.5 µM of each primer, in a volume of 100 µl of Taq polymerase reaction mixture containing 10 µl PCR Buffer, 0.5 mM of each dNTP and 2.5 mM $MgCl_2$. Amplification was performed using the following cycling scheme:

1. 5 cycles of: 95.0°C - 30", 55°C - 30", 72°C - 10'
2. 35 cycles of: 95.5°C - 30", 50°C - 30", 72°C - 8'

The PCR fragments of the expected length for NgoMI and StuI treated and then ligated chromosomal DNA were digested with either BamHI or Sau3a and cloned into pUC19 : BamHI and pUC19:(BamHI+SmaI) and sequenced with CircumVent Thermal Cycle DNA sequencing kit. The 1.6kb (BamHI+BamH) fragment from the NgoMI PCR product contained a sequence coding for the N-terminal part of *DnaN*, followed by the gene for enolase. The 1kb (Sau3a+Sau3a) fragment from the same PCR product included the start of *dnaN* gene and sequence characteristic of the origin of replication (i.e. 9mer DnaA-binding site sequences). The 0.6kb (BamHI+BamHI) fragment from the StuI PCR reaction contained starts for dnaA and gidA genes in inverse orientation to each other. The 0.4 kb (Sau3a+Sau3a) fragment from the same PCR product contained the 3' end of the *dnaA* gene and DNA sequence characteristic for the origin of replication.

Please replace the paragraph beginning at page 88, line 21, with the following amended paragraph:

Cloning and sequence of the *dnaA* gene - The dnaA gene was cloned for sequencing in two parts: from the potential start of the gene up to its middle and from the middle up to the end. For the N-terminal part the upstream 27mer (5'-TCTGGCAACACGTTCTGGAGCACATCC-3') (SEQ ID NO: 54) was 20 bp downsteam of the potential start codon of the gene. The downstream 23mer (5'-TGCTGGCGTTCATCTTCAGGATG-3') (SEQ ID NO: 55) was approximately from the middle of the dnaA gene. For the C-terminal part the upstream 23mer (5'-CATCCTGAAGATGAACGCCAGCA-3') (SEQ ID NO: 56) was complementary to the previous primer. The downstream 25mer (5'-AGGTTATCCACAGGGGTCATGTGCA-3') (SEQ ID NO: 57) was 20 bp upstream the potential stop codon for the dnaA gene. The amplification reactions contained 10 ng *T.th.* genomic DNA, 0.5 µM of each primer, in a volume of 100 µl of Vent polymerase reaction mixture containing 10 µl ThermoPol Buffer,

0.5 mM of each dNTP and 0.5 mM $MgSO_4$. Amplification was performed using the following cycling scheme:

1. 5 cycles of: 95.5°C - 30", 55°C - 30", 75°C - 3'
2. 30 cycles of: 95.5°C - 30", 50°C - 30", 75°C - 2'

Products were visualized in a 1.0% native agarose gel. Fragments of the expected sizes of 750 bp and 650 bp were produced, and were sequenced using CircumVent Thermal Cycle DNA sequencing method (New England Biolabs). The nucleotide and amino acid sequences of *dnaA* and its protein product are shown in Fig. 20. The *DnaA* protein is homologous to the *DnaA* proteins of several other bacteria as shown in Fig. 19.

Please replace the paragraph beginning at page 89, line 16, with the following amended paragraph:

Cloning and expression of *dnaN* - The full length *dnaN* gene was obtained by PCR from *T.th.* total DNA. DNA oligonucleotides for amplification of *T.th. dnaN* were the following: the upstream 29mer (5'-GTGTGTCATATGAACATAACGGTTCCCAA-3') (SEQ ID NO: 58) consists of an NdeI site within first 11 nucleotides (underlined), followed by the sequence for the start of the *dnaN* gene; the downstream 29mer (5'-GCGCGAATTCTCCCTTGTGGAAGGCTTAG-3') (SEQ ID NO: 59) consists of an EcoRI site within the first 10 nucleotides (underlined), followed by the sequence complementary to a section just downstream of the *dnaN* stop codon. The amplification reactions contained 10 ng T.th. genomic DNA, 0.5 μM of each primer, in a volume of 100 μl of Vent polymerase reaction mixture containing 10 μl Thermopol Buffer, 0.5 mM of each dNTP and 0.2 mM Mg SO_4. Amplification was performed using the following cycling scheme:

1. 5 cycles of: 95.0°C - 30", 55°C - 30", 75°C - 5',
2. 35 cycles of: 95.5°C - 30", 50°C - 30", 75°C - 4'.

The nucleotide and amino acid sequences of *dnaN* and the ß subunit, respectively, are shown in Fig. 21. The *T.th.* ß subunit shows limited homology to the ß subunit sequences of several other bacteria over its entire length (Fig. 22).